REMARKS

Applicants acknowledge receipt of the Office Action mailed November 16, 2010, and note the withdrawal of the obviousness rejections of claims 1, 16, 18-19, and 21-23 over Hamdi in view of Katori. Reconsideration and withdrawal of the currently outstanding rejections is respectfully requested.

The Examiner is thanked for the courtesy and consideration shown at the Interview held on February 10, 2011, during which the outstanding rejections were discussed.

In support of the patentability of the presently claimed invention, Applicants enclose a Rule 131 Declaration of Dr. Veronique Coxam ("Coxam Decl.").

Claim 1 has been amended to more particularly point out that the claimed method is performed on subjects who suffer from unbalanced bone formation/bone resorption ratio. This amendment is supported in the specification at page 14, lines 25-29. No new matter has been added.

Claims 1-2, 4-5, 7-14, 16, 18-19, 21-23, and 25-26 are pending and under consideration. Claims 3, 6, 15, 17, 20, and 24 have been withdrawn from consideration.

Anticipation Rejection over Hamdi

The Examiner has rejected claims 1-2, 4-5, 7-14, 16, 18-19, and 21-23 under 35 U.S.C. § 102(b) as allegedly anticipated by Hamdi, et al., U.S. Patent Application Publication US 2003/0004117 ("Hamdi"). The Examiner states:

> "Hamdi et al teach methods for inhibiting angiogenesis comprising administering oleuropein and/or the products of its hydrolysis in therapeutically effective amounts. Since oleuropein is present in therapeutically effective amounts, it reads on "active compound." The methods and compositions are particularly effective in inhibiting the vascularization of endothelial cells, and may be utilized to treat a wide variety of cancers,

> ocular discases, and inflammatory conditions. The populations to which the compositions of Hamdi are administered are the same as those of the claimed invention, since persons being treated for cancers, ocular diseases, and inflammatory conditions would also seek to prevent bone loss which occurs with aging, and/or seek to prevent a disorder associated with unbalanced bone formation-bone resorption ratio, and/or might suffer from a condition such as type I or type II osteoporosis or secondary osteoporosis...Therefore, since the same composition (i.e. a composition comprising oleuropein as active compound) is administered to the same population(s) in the same amount, the same effect(s) would necessarily take place, i.e. stimulation of bone formation and/or inhibition of bone resorption. Therefore, the invention of Hamdi anticipates the claimed invention."

(Office Action, p. 4). Applicants traverse, and respectfully submit that the Examiner has misapplied the law to the facts of this case.

As is undoubtedly known to the Examiner, it is well established that new uses of old products are patentable subject matter. *See* 35 U.S.C. § 101 (identifying as patentable "any new and useful improvements" of a process, machine, manufacture, etc.); *see, also In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986) (principles of inherency do not prohibit a process patent for a new use of an old structure). In this vein, new medical uses for old compounds and compositions are clearly patentable, as is the case with the present claims.

As has been pointed out in previous amendments, and as acknowledged by the Examiner, Hamdi neither teaches nor suggests that oleuropein may induce bone formation and/or inhibit bone resorption. Hamdi discusses the effect of oleuropein on angiogenesis, but does not even mention bone formation/resorption at all. Hamdi identified over 40 different diseases which may be treated with its method, none of which relate to bone metabolism (¶¶ 60-62).

In fact, angiogenesis (the focus of Hamdi) and bone metabolism (the focus of the present invention) are, biologically, very distinct. For example, as discussed in detail in the last Amendment, COX-2 inhibitors – which are anti-angiogenic compounds – may have no effect on, or may even severely inhibit, bone formation.

Therefore, as a preliminary matter, it is clear that Hamdi does not teach the use of oleuropein to stimulate bone formation and/or inhibit bone resorption. The Examiner, recognizing this, has in essence argued that Hamdi inherently anticipates the presently claimed method. However, both the law on inherency and the facts of this case make it clear that Hamdi cannot inherently anticipate the present claims.

As the Examiner knows, in considering a possible anticipation rejection, even if the prior art does not expressly disclose all of the limitations of the claimed invention, it may anticipate that invention if the limitations are inherent in the disclosure of the prior art. *See, e.g.*, MPEP 2112. The Federal Circuit has articulated the law on inherency as follows:

> A single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation. Thus, a prior art reference without express reference to a claim limitation may nonetheless anticipate by inherency. Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claims limitations, it anticipates.

Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1376 (Fed. Cir. 2005) (emphasis added, internal citations omitted.)

However, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *see, also In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). As the Federal Circuit has stated:

> "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the

> thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing ***may*** result from a given set of circumstances is not sufficient.' "

In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (emphasis added, internal citations omitted); see also, MPEP 2112.IV.

In this case, the Examiner has asserted that because Hamdi's method might be used on patients who suffered from osteoporosis, it inherently anticipates the presently claimed invention. However, as the foregoing case law makes clear, in order to inherently anticipate, the prior art must necessarily (i.e. always) result in the claimed invention. The mere fact that the presently claimed invention might result from carrying out Hamdi's method is not sufficient to establish inherency.

In this regard, it is important to recall that the presently claimed method requires administration of oleuropein to a subject suffering from unbalanced bone/bone resorption ratio. Even if some of the patients suffering from the diseases identified by Hamdi as being susceptible to treatment using his method are in need of stimulating bone formation and/or inhibiting bone resorption, it is clear that not all would be. There is no evidence that a person suffering from ocular diseases, cancers, and inflammatory disorders would necessarily be a subject in need of simulation of bone formation and/or inhibition of bone resorption and in particular, a patient suffering from unbalanced bone formation/bone resorption ratio.

As stated by Dr. Coxam in her Declaration the diseases discussed in Hamdi are unrelated to an unbalance of bone metabolism and can affect a large variety of people independently of their bone status and their age (Coxam Decl. ¶ 11).

In other words, the universe of patients suffering from the conditions set forth by Hamdi will encompass persons who do not actually need to induce bone formation and/or the inhibit bone resorption. Such persons include, for example, patients suffering from genetic diseases due to low bone resorption activity or people with balanced bone metabolism. In the same way, patients suffering from an unbalanced bone formation/bone resorption ratio, as defined in presently pending claim 1, do not necessarily need inhibition of angiogenesis and do not necessarily suffer from the pathologies listed in Hamdi. In other words, there is no correlation between the patients of Hamdi and the patients targeted by the claimed method.

Accordingly, Hamdi fails to disclose, even implicitly, the group of patients defined in the present invention, which is one of the main feature of the claimed method. The anticipation rejection based on inherency must thus be withdrawn.

This facts in this case are analogous to the facts in *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F. 3d 1362 (Fed. Cir. 1999). In that case, claim 1 of the patent at issued included the step of "aligning a laser light applicator substantially vertically over a hair follicle opening." 192 F. 3d 1365. The prior art under consideration did not discuss hair follicles at all, much less aligning a laser over a hair follicle opening. *Id.* Therefore, the prior art did not explicitly teach alignment substantially vertically over a follicle opening. The Court then considered whether this limitation was inherent in the prior art:

> The [prior art] teaches aiming the laser at skin pigmented with tattoo ink. The record discloses no necessary relationship between the location of a tattoo and the location of hair follicles. Therefore, an operator of the RD-1200 laser could use the laser according to the manual without necessarily aligning the laser "substantially vertically over a hair follicle opening." The possibility of such an alignment does not legally suffice to show anticipation. See *In re Oelrich*, 666 F.2d at 581. Occasional results are not inherent. Because this court holds that the manual does not inherently teach this limitation of the claimed invention, it does not address MEHL/Biophile's other arguments. To anticipate, a single reference must teach every limitation of the claimed invention. Without an inherent

> teaching about alignment, [**9] the manual does not anticipate the claimed invention.

Id. (emphasis added). Thus, the Court held that although it was possible that the prior art might meet the limitation at issue, because it did not necessarily do so (*i.e.* always do so), it could not inherently anticipate the claims at issue. Similarly, although Hamdi's method could be practiced on subjects who are suffering from unbalanced bone formation/bone resorption ratio, it does not necessarily do so. Accordingly, the law requires withdrawal of the anticipation rejection. *MEHL/Biophile Int'l Corp.; In re Robertson.*

For all of the foregoing reasons, Applicants respectfully submit that the anticipation rejection over Hamdi should be reconsidered and withdrawn.

Rejection over Lockwood in view of Nachman

The Examiner has rejected claims 1-2, 4-5, 7-14, 16, 18-19, 21-23, and 25-26 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lockwood, U.S. Patent No. 7,445,807 ("Lockwood") as evidenced by Nachman, U.S. Patent No. 5,714,150 ("Nachman"). According to the Examiner:

> "Lockwood teaches agglomerated granular protein-rich nutritional supplements, for use by specific groups of individuals. Lockwood teaches that one group to be treated include [sic] postmenopausal women, who are particularly susceptible to osteoporosis, and teaches supplements designed for women. The supplements may comprise edible plant extracts, including olive leaf extract. Olive leaf extract is know to inherently contain oleuropein; as evidence Nachman teaches a method of producing olive leaf extract known as oleuropein with valuable medicinal properties, including antiviral activity, and therefore reasonably reads on "active compound." Therefore, one skilled in the art of edible plant extracts would envisage oleuropein from the disclosure of "olive leaf extract" in Lockwood, and thus the composition of Lockwood reads on "a composition comprising oleuropein as active compound" as taught in claim 1.
>
> "While Lockwood teaches a composition comprising edible plant extracts which may be olive leaf extract (which inherently contains oleuropein), Lockwood does not specifically exemplify a composition comprising olive leaf extract sufficient to anticipate the claimed invention.
>
> "Nachman teaches a method of producing olive leaf extract known as oleuropein with valuable medicinal properties, including anti-viral properties.

> "It would have been obvious to a person having ordinary skill in the art at the time the invention was made to select olive leaf extract as the edible plant extract in the composition of Lockwood, since the olive leaf extract provides the benefits of valuable medicinal properties, including anti-viral properties, as taught by Nachman. Therefore, one skilled in the art would be motivated to select olive leaf extract from the list of edible plant extracts taught by Lockwood for inclusion in its composition, in order to improve the overall health of those taking the composition, including persons of disparate ages, genders, and levels of physical activity.
>
> Additionally, while Lockwood does not specifically teach that the supplement comprising olive leaf extract stimulates bone formation and/or inhibits bone resorption, the populations to which the compositions of Lockwood are administered are the same as those of the claimed invention, since all persons of disparate genders, ages, and levels of physical activity would seek to prevent bone loss which occurs with aging, and/or seek to prevent a disorder associated with unbalanced bone formation-bone resorption ratio, and/or might suffer from a condition such as type I or type II osteoporosis or secondary osteoporosis.

(Office Action, pp. 7-8, internal citations omitted). Applicants respectfully traverse.

In making this rejection, the Examiner is again relying on principals of inherency, arguing that all persons would seek to prevent bone loss. This argument again fails to account for the fact that the claims recite a method which comprises administering oleuropein to subjects who are suffering from unbalanced bone formation/bone resorption ratio. It is undisputed that not everyone suffers from unbalanced bone formation/bone resorption ratio. Therefore, for all of the reasons discussed above in connection with the anticipation rejection over Hamdi, Applicants submit that the presently claimed invention cannot be reconstructed from Lockwood using an inherency argument. Simply put, although it is possible to partly reconstruct the invention – after the fact – from Lockwood and Nachman, such a reconstruction cannot be made without reference to the invention.

Thus, the Examiner's rejection is, in Applicants' view, ultimately based on a hindsight-based reconstruction of the claimed invention, and is dependent on a number of assumptions/propositions which are not necessarily correct.

Additionally this reconstruction lacks the essential characteristic related to the population to be treated, namely patients suffering from an unbalanced bone formation/bone resorption ratio.

First, Lockwood's dietary supplement does not necessarily comprise "edible plant extracts," as shown at column 11, lines 16-18 (reciting that the amount of edible plant extract in the composition can be zero).

Second, even if an edible plant extract is used, Lockwood provides no motivation to specifically use olive leaf extracts, which are mentioned as one of over 45 possible choices (col. 9, lines 28-37). That Nachman teaches that oleuropein might have anti-viral properties is of no moment. Lockwood makes clear that all of the edible plant extracts which could be used in its composition have useful properties (see, col. 4, lines 30-39). Thus, that oleuropein might have useful properties provides no reason to select olive leaf extract over the other 45+ listed possibilities for preparing nutritional supplements.

Third, Nachman teaches that oleuropein is an antiviral agent, which would be of no significance in improving the nutritional status of patients as sought by Lockwood. Thus, a person of skill in the art reviewing Lockwood would have no reason to specifically select olive leaf extract as the edible plant extract for use in the described nutritional supplement. This point is discussed in more detail in the Coxam Declaration at ¶14.

Fourth, there is no proof that the olive leaf extracts described by Lockwood even contain oleuropein. This is because oleuropein is not an inherent compound present in all olive leaf extracts. As illustrated by Nachman, oleuropein is a minor component in olive leafs since it generally accounts for about 0.30% by weight in olive leaves (see, col. 2, lines 28-31). The presence of oleuropein in olive leaf extract depends on (i) the origin of olive leafs, (ii) the conditioning of olive leafs prior to its extraction, (iii) the extraction process used (in particular the temperature and the solvent of extraction) and (iv) the storage of the extract prior to its use (Coxam Decl. ¶ 15). Depending on the extraction process used, it is possible to obtain an olive leaf extract devoid of oleuropein. Id. Since Lockwood neither indicates the kind of olive leaf extracts to be used nor mentions oleuropein as a compound of interest, the nutritional supplement of Lockwood, even if prepared from olive leaves, does not necessarily contain oleuropein. In other words, it is evident that the nutritional supplement of Lockwood does not necessarily (i.e. always) result in the claimed invention.

Finally, Applicants reiterate that the presently claimed invention is not a composition, but instead is a method for stimulating bone formation and/or inhibiting bone resorption comprising the administration of oleuropein to a subject in need thereof. Neither Lockwood nor Nachman (nor Hamdi) teach or suggest administering oleuropein in this manner, requiring withdrawal of the rejection.

Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance, and earnestly solicit prompt notice to that effect. Should the Examiner believe a personal interview would be helpful in advancing prosecution, he is invited to telephone the undersigned.

Respectfully submitted,

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